Prenatal care: Patient education, health promotion, and safety of commonly used drugs

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INTRODUCTION

Prenatal care in the first few prenatal visits involves a substantial amount of patient education and health promotion. This topic will discuss routine patient education and health promotion in early pregnancy and use of common medications across pregnancy. Other important aspects of prenatal care are reviewed separately. (See "Prenatal care: Initial assessment" and "Prenatal care: Second and third trimesters".)

PATIENT EDUCATION AND HEALTH PROMOTION

Practice issues — Women should be informed about the following:

- When to call the provider (eg, vaginal bleeding or change in vaginal discharge, leakage of fluid from the vagina, fever, pain, vomiting, acute shortness of breath, calf or leg pain, headache, visual changes, dysuria, pruritus, uterine contractions, crampy abdominal pain, decreased fetal activity [after perception of fetal activity has become established], fainting or dizziness, or personal concern about a change in health status).
- How to reach the provider after business hours, coverage arrangements, and the role of various office personnel.
- The hospital where delivery will occur.

- Confidentiality issues (eg, information left on phone answering machines, use of electronic mail, and discussions with family members). There should be an explanation of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and how it affects the patient (information is available at www.hhs.gov/ocr/hipaa/).

Diet, supplements, and weight gain

Vitamins and minerals — A standard prenatal multivitamin with iron and folic acid satisfies the daily vitamin and mineral requirements of most pregnant women. Although prenatal multivitamin use has not been proven to improve maternal and neonatal outcomes in high income countries like the United Kingdom, where women are typically well-nourished and food is vitamin-fortified, in the absence of a careful evaluation of a pregnant woman's nutritional status or consultation with a nutritionist, we believe it is prudent to recommend one prenatal multivitamin daily. Micronutrient supplementation is discussed in more detail separately. (See "Nutrition in pregnancy", section on 'Micronutrients'.)

The multivitamin should contain iron 15 to 30 mg to prevent iron deficiency; the Centers for Disease Control and Prevention (CDC) recommends 30 mg/day to achieve the 30 mg Recommended Daily Allowance for pregnant women [1]. However, if daily intake of a multivitamin containing iron is poorly tolerated, a vitamin without iron and intermittent iron supplementation (one to three times per week) appears to be as effective as daily supplementation for preventing anemia at term and is better tolerated [2]. Gastrointestinal distress is common at doses of 45 mg/day [3]. (See "Nutrition in pregnancy", section on 'Iron'.)

The multivitamin should also contain folic acid 0.4 to 0.8 mg to reduce the risk of open neural tube defects during the period of neural tube closure. Folic acid may have pregnancy benefits unrelated to prevention of neural tube defects, but available data are insufficient to support a clear benefit. (See "Folic acid supplementation in pregnancy".)

Some experts advise high-dose vitamin D supplementation (eg, 2000 to 4000 international units/day) in addition to the Recommended Dietary Allowance for women whose children are deemed at high risk of asthma (eg, both parents have asthma) [4]. (See "Risk factors for asthma", section on 'Vitamin D'.)

Diet, including food safety — Nutrition, special diets, food safety, use of nonnutritive sweeteners, as well as foods/supplements that should be consumed (eg, folic acid), limited (eg, caffeine), or avoided (eg, most herbal products, fish high in mercury (table 1)) are discussed in detail separately.

- (See "Nutrition in pregnancy".)

- (See "Fish consumption and marine omega-3 fatty acid supplementation in pregnancy".)
- (See "Primary prevention of allergic disease: Maternal diet in pregnancy and lactation".)
- (See "The effects of caffeine on reproductive outcomes in women".)
- (See "Treatment and prevention of Listeria monocytogenes infection", section on 'Prevention of foodborne infection'.)

General principles of food safety in pregnancy include the following [5-7]:

- Wash fruits and vegetables before eating raw or cooking.
- Avoid unpasteurized juice, cider, and milk (including soft cheese [eg, some Brie, Camembert, Roquefort, feta, queso blanco or queso fresco] and other products made with raw milk).
- Avoid premade meat or seafood salad (eg, deli chicken, ham, or tuna salad).
- Avoid raw sprouts.
- Avoid possibly contaminated water. (In the United States, public water drinking systems ensure safety using a combination of disinfection, coagulation, flocculation, sedimentation, and filtration.)
- Avoid undercooked meat, poultry, fish, and eggs. Cook to the United States Department of Agriculture (USDA)-recommended minimum safe internal temperature.
- Avoid or limit consumption of fish with elevated levels of mercury (table 1). (See "Fish consumption and marine omega-3 fatty acid supplementation in pregnancy", section on 'Methylmercury in fish'.)
- Avoid refrigerated smoked seafood (which could be contaminated with listeria) unless it is in a cooked dish, such as a casserole.
- Reheat hot dogs and luncheon meats/cold cuts/fermented or dry sausage, even though precooked.
- Avoid refrigerated pâtés or meat spreads from a deli or meat counter or from the refrigerated section of a store.
- Avoid raw dough.
- Avoid or limit caffeine to <200 mg/day (usually equivalent to ≤3 cups/day).

Also:

- Wash cutting boards, dishes, counters, and utensils with hot, soapy water after contact with raw meat, poultry, seafood, or unwashed fruits or vegetables.
- Wash hands with soap and water before and after food preparation.
- Freezing meat for several days at subzero (0°F) temperatures before cooking greatly reduces the chance of infection.
- Avoid accidental contact of cat feces through touching hands to mouth after gardening, handling cats, cleaning a cat's litter box, or touching anything that has come into contact with cat feces.

Gestational weight gain — Recommendations for gestational weight gain are based on prepregnancy body mass index (table 2). Pregnancy is a risk factor for excessive weight gain, which increases future risks of cardiovascular disease and diabetes. Both excessive weight gain and obesity have been associated with an increased risk of cesarean delivery and macrosomia. Prenatal care is an important opportunity for discussing these risks and counseling about diet and exercise to achieve an appropriate weight gain. (See "Gestational weight gain" and "Obesity in pregnancy: Complications and maternal management".)

Healthy behaviors

Use of seat belts and air bags — Pregnant women should continue wearing three-point seat belts when traveling during pregnancy. The lap belt is placed across the hips and below the uterus; the shoulder belt goes between the breasts and above and lateral to the uterus. Although there are case reports of maternal and fetal injuries resulting from seat belt use, the overall effect is that seat belts provide significantly more benefit than risk to the mother and fetus in the event of collision [8,9].

There is less evidence regarding the effects of air bags. The largest study was a retrospective cohort study that assessed the effect of air-bag availability and air-bag deployment on the risk of adverse pregnancy outcome in over 3000 pregnant, front-seat occupants in motor vehicle crashes in Washington State [10]. Almost all women wore seat belts; two-thirds were in air bag equipped vehicles and one-third of the women were in vehicles without airbags. For the entire cohort, the authors did not find a statistically significant association between the presence of an air bag in the vehicle and risk of any adverse maternal or perinatal outcome in the event of a crash. When they compared only those crashes where an air bag deployed with those where it would have been likely to deploy if the vehicle was equipped with one, they found air bag deployment was associated with a trend toward increased preterm labor (relative risk [RR] 1.7, 95% CI 0.9-3.2), but not preterm birth (RR 0.8, 95% CI 0.3-1.9). The number of women with

placental abruption or fetal death was too small to provide meaningful comparisons (abruption 4/198 with airbag deployed versus 10/622 without deployed air bag; fetal death 2/198 versus 2/622).

The American College of Obstetricians and Gynecologists (ACOG) recommends that pregnant occupants of motor vehicles wear lap and shoulder seatbelts and should not turn off air bags [11].

Oral health — Prevention, diagnosis, and treatment of oral conditions should not be deferred because of pregnancy. Dental radiographs (with shielding of the abdomen and thyroid) and procedures such as local anesthesia, dental extraction, root canal, restoration (amalgam or composite) of untreated caries, flossing, and scaling/root planing of plaque/biofilm are not harmful to the fetus. As many dentists are reluctant to provide care beyond routine cleaning in pregnancy, obstetricians should be willing to provide patients with letters or other references to support the provision of appropriate dental care.

Oral Health Care During Pregnancy: A National Consensus Statement is a helpful online resource that provides information by an expert workgroup convened by the Health Resources and Services Administration (HRSA) in collaboration with ACOG and the American Dental Association (ADA).

Avoidance of alcohol, cigarettes, and misuse of drugs — Maternal alcohol consumption, smoking, or misuse of drugs can be harmful to the fetus. Ideally, pregnant women will completely stop using these substances. Patients should be strongly advised of the risks of this behavior and referred to cessation or substitution programs in their area.

- (See "Alcohol intake and pregnancy".)
- (See "Cigarette and tobacco products in pregnancy: Impact on pregnancy and the neonate".)
- (See "Tobacco and nicotine use in pregnancy: Cessation strategies and treatment options".)
- (See "Substance use during pregnancy: Screening and prenatal care".)
- (See "Overview of management of opioid use disorder during pregnancy".)
- (See "Methadone and buprenorphine pharmacotherapy of opioid use disorder during pregnancy".)

Exercise and physical activity — For most pregnant women with uncomplicated pregnancies, the following exercise prescription is reasonable and part of a healthy lifestyle: moderate-intensity exercise (able to carry on a normal conversation during exercise) that includes aerobic exercise and strength training, performed for 30 minutes daily, five to seven days per week. Issues regarding type, frequency, and duration of exercise, as well as risks of

and contraindications to exercise, are reviewed separately. (See "Exercise during pregnancy and the postpartum period".)

Although widely believed to improve some pregnancy outcomes, there is no high quality evidence that bed rest reduces the risk of miscarriage, preterm birth, or preeclampsia or improves pregnancy outcome in multiple gestation or impaired fetal growth [12-15]. Moreover, bed rest has known potential harms: It promotes loss of trabecular bone density, increases venous thromboembolism risk, produces musculoskeletal deconditioning, and places significant psychosocial strain on individuals and families [16-23].

Hot tubs, saunas, and pools — Hot tubs and saunas probably should be avoided during the first trimester because maternal heat exposure leading to hyperthermia has been associated with an increased risk of neural tube defects, and possibly other birth defects [24]. At a minimum, exposure should be short so that core temperature does not increase. (See "Open neural tube defects: Risk factors, prenatal screening and diagnosis, and pregnancy management", section on 'Fever/hyperthermia'.)

In a population-based study, swimming pool use did not appear to have any teratogenic effects despite exposure to water disinfection products and potential water-borne pathogens [25].

Precautions against infection — Some infections are potentially harmful in pregnancy and interventions should be taken to minimize the risk of these infections. In general, pregnant women should avoid contact with people with febrile illnesses that could be contagious and should practice good hygiene.

Immunization

- **Influenza** – Influenza vaccination is recommended for women who are or will be pregnant during the influenza season, regardless of stage of pregnancy. (See "Seasonal influenza and pregnancy", section on 'Vaccination'.)

- **Tetanus, diphtheria, pertussis** – Tetanus and diphtheria immunizations and boosters should be up-to-date. (See "Immunizations during pregnancy", section on 'Tetanus, diphtheria, and pertussis vaccination'.)

  The tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine is administered in the third trimester of each pregnancy to protect the infant from pertussis, regardless of prior vaccination.

- Other vaccinations are shown in the table (table 3).

Preventive measures for other infections

- **Sexually transmitted infections** – Since there is no need for contraception in pregnancy, many women do not consider using condoms with sexual activity. For patients who may be at high risk of exposure (table 4) to sexually transmitted infections, clinicians should discuss condom use during pregnancy to reduce this risk.

- **Toxoplasmosis** – Prevention of primary infection is based on avoidance of sources of infection, which include ingestion of contaminated, undercooked, or cured meat or meat products; soil-contaminated fruits or vegetables; or contaminated unfiltered water. Routine screening is performed in some countries but not the United States. (See "Toxoplasmosis and pregnancy", section on 'Prevention'.)

- **Cytomegalovirus** – Prevention of primary cytomegalovirus infections is based on good personal hygiene throughout pregnancy, especially hand washing with soap and water after contact with diapers or oral and nasal secretions (particularly with a child who is in daycare), not kissing children under age 6 on the mouth or cheek; not sharing food, drinks, or oral utensils with young children; and cleaning toys, countertops, and other surfaces that come into contact with children's urine or saliva. (See "Cytomegalovirus infection in pregnancy", section on 'Strategies for prevention of maternal and/or fetal infection'.)

- **Varicella** – Prevention is based on prepregnancy immunization and avoidance of significant exposure to varicella infection, which is highly contagious. The United States Advisory Committee on Immunization Practices recommends VariZIG, a varicella-zoster immune globulin preparation, in all nonimmune pregnant women who have been exposed to persons with varicella. (See "Varicella-zoster virus infection in pregnancy" and "Vaccination for the prevention of chickenpox (primary varicella infection)".)

- **Parvovirus** – Young children are the main source of respiratory-acquired parvovirus B19. The best measures to prevent maternal infection are good personal infection control practices, such as hand hygiene; not touching the eyes, mouth, or nose; avoiding close contact with sick individuals; and teaching children to cover their mouth and nose with an elbow or tissue when sneezing or coughing. Many pregnant women have preexisting immunoglobulin G (IgG) to the virus, indicating immunity from a prior infection; those who are exposed to or have symptoms of parvovirus infection should have serologic testing for IgG and IgM antibodies, and if acutely infected, they should be monitored for fetal effects. (See "Parvovirus B19 infection during pregnancy" and "Treatment and prevention of parvovirus B19 infection".)

- **Zika** – Given an association between Zika virus exposure during pregnancy and congenital microcephaly, pregnant women are advised to consider postponing travel to areas with ongoing mosquito transmission of Zika virus [26]. Women who must travel are advised to take precautions against mosquito bites, including wearing long-sleeved shirts and pants, staying in places with air conditioning, sleeping under a mosquito net, and using an approved insect repellant. In addition, pregnant women whose sexual partner has traveled to affected regions should abstain from sexual activity (vaginal, anal, and oral sex) or use condoms for the duration of the pregnancy. (See "Zika virus infection: Evaluation and management of pregnant women", section on 'Guidance for pregnant women'.)

- **Infections associated with pets** – Women who are pregnant or planning pregnancy should avoid contact with all rodents [27]. Precautions about handling pets and laboratory animals are discussed in topic reviews on each animal. Refer to topic reviews on zoonotic infection separately. (See "Zoonoses from cats" and "Zoonoses from dogs" and "Zoonoses from pets other than dogs and cats".)

- **Listeria and other foodborne infections** – To reduce the risk of foodborne illness, it is important that pregnant women practice good personal hygiene (frequent hand washing); consume only meats, fish, and poultry (including eggs) that are fully cooked; avoid unpasteurized dairy products and fruit/vegetable juices; thoroughly rinse fresh fruits and vegetables under running water (approximately 30 seconds) before eating; avoid eating raw sprouts (including alfalfa, clover, radish, and mung bean); and wash hands, food preparation surfaces, cutting boards, dishes, and utensils that come into contact with raw meat, poultry, or fish using hot, soapy water. (See "Treatment and prevention of Listeria monocytogenes infection", section on 'Prevention of foodborne infection'.)

- **Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)** – SARS-CoV-2 is the virus that causes coronavirus disease 2019 (COVID-19). Pregnant women should follow the same recommendations as nonpregnant persons for avoiding exposure to the virus (eg, social distancing, hand hygiene, disinfecting surfaces, wearing a mask in public). (See "COVID-19: Epidemiology, virology, and prevention" and "COVID-19: Pregnancy issues and antenatal care".)

Sleep position — Pregnant women tend to avoid the supine position when awake because of associated symptoms (table 5), but it appears that many spend some time sleeping supine [28]. The supine position in late pregnancy can decrease cardiac output and uterine perfusion due to aortocaval compression from the gravid uterus. Although the supine position during sleep in late pregnancy has been associated with an increased risk for stillbirth in case-control

studies [29-32], limitations of such studies include potential recall bias and confounding factors that may influence both sleep position, sleep pattern, and stillbirth.

A large prospective multicenter cohort study evaluating maternal sleep position and subsequent adverse pregnancy outcomes reported that women whose objectively measured sleep position was supine at least 50 percent of the time at 22 to 30 weeks were not significantly more likely to have the composite adverse outcome than those in the supine position ≤50 percent of the time (composite adverse outcome: stillbirth, small for gestational age newborn, and gestational hypertensive disorders, odds ratio [OR] 1.24, 95% CI 0.98-1.57) [33]. In particular, the frequency of stillbirth in women sleeping in the non-left lateral and left lateral position was 5/4667 (0.1 percent) and 13/3511 (0.4 percent), respectively (OR 0.27, 95% CI 0.09-0.75), which should reassure women that they can sleep in the positions in which they are most comfortable. (See "Maternal adaptations to pregnancy: Cardiovascular and hemodynamic changes", section on 'Postural hypotensive syndrome'.)

Intimate partner violence — Intimate partner violence may escalate during pregnancy or the postpartum period and has been associated with a variety of adverse maternal and pregnancy outcomes. Providers should screen for intimate partner violence at periodic intervals and make available take-home resource materials, such as safety procedures, hotline numbers, and referral information that the patient can access privately [34]. (See "Intimate partner violence: Epidemiology and health consequences" and "Intimate partner violence: Diagnosis and screening" and "Intimate partner violence: Intervention and patient management".)

Common patient concerns

Risk of birth defects and inherited disorders — The prevalence of birth defects of medical, surgical, or cosmetic significance is 2 to 4 percent among liveborn infants and does not vary among ethnic groups. Both genetic and environmental factors play a role in pathogenesis. (See "Birth defects: Causes".)

The clinician should discuss the causes of congenital anomalies and risk for inherited disorders with the patient, assess the specific risk for the child, review options for and limitations of prenatal diagnosis, and decide whether additional testing and referral to a geneticist would be useful.

- (See "Down syndrome: Overview of prenatal screening".)
- (See "Expanded carrier screening in pregnant women and women planning pregnancy".)
- (See "Preconception and prenatal carrier screening for genetic disease more common in the Ashkenazi Jewish population and others with a family history of these disorders".)

- (See "Open neural tube defects: Risk factors, prenatal screening and diagnosis, and pregnancy management".)
- (See "Prenatal screening and testing for hemoglobinopathy".)

Employment issues — A woman with an uncomplicated pregnancy who is employed where there are no greater potential hazards than those encountered in routine daily life may continue to work without interruption until the onset of labor. However, workplace safety and the physical demands of the woman's job should be considered, especially in women at higher risk of preterm delivery. (See "Working during pregnancy".)

Sexual activity — Theoretically, sexual intercourse may stimulate labor due to physical stimulation of the lower uterine segment, endogenous release of oxytocin as a result of orgasm, direct action of prostaglandins in semen, or increased exposure to infectious agents. However, in the absence of pregnancy complications (eg, vaginal bleeding, ruptured membranes), there is insufficient evidence to recommend against sexual intercourse during pregnancy. Most studies have not shown an increased risk of preterm labor/delivery or infectious complications, unless a sexually transmitted disease is acquired [35,36].

Travel — Pregnant women who travel need to consider several issues, including:

- Their risk of pregnancy complications away from their usual source of medical care, as well as the availability of medical resources and their medical insurance coverage at their destination.
- The increased risk of venous thromboembolism during pregnancy and with prolonged immobility during the trip.
- Issues related to air travel (eg, access to medical providers, lower oxygen environment, restricted movement). (See 'Airline travel' below.)
- The potentially increased risk of exposure to infectious diseases (eg, travelers' diarrhea, malaria, Zika virus, SARS-CoV-2), as well as prophylaxis, prevention, and treatment of these diseases. Given the association between Zika virus during pregnancy and congenital microcephaly, pregnant women should consider postponing travel to areas with mosquito-borne Zika virus transmission. (See "Zika virus infection: Evaluation and management of pregnant women".)

The American College of Obstetricians and Gynecologists and the European Board and College of Obstetrics and Gynaecology are among the organizations that have published guidance for pregnant travelers [37,38].

Airline travel — Most airlines allow women to fly up to 37 weeks of gestation with singleton pregnancies and up to 32 weeks with twin pregnancies, although individual policies may vary, so women should check with their airline. Commercial airline travel is generally safe for women with uncomplicated pregnancies [37,39-42]. Fetal heart rate is not affected during the flight if the mother and fetus are healthy [40].

A review of observational studies reported an increased risk of miscarriage in flight attendants (OR 1.62, 95% CI 1.29-2.04) and an increased risk of preterm birth among passengers (OR 1.44, 95% CI 1.07-1.93) [43], particularly women who fly for long durations and frequently [44]; however, in contrast to passengers, flight attendants do not appear to have an increased risk of preterm birth [43]. These discordant findings could be due to failure to account for relevant differences between study subjects and controls.

Maternal physiologic adaptations to the reduced barometric pressure at high altitude include hemoconcentration, increased heart rate and blood pressure, and decreased aerobic capacity with reduction of partial oxygen pressure [40,45] (see 'Travel to moderate and high altitudes' below). For these reasons, certain precautions are suggested during air travel [37]:

- Maintain hydration and regularly move lower extremities to minimize stasis and reduce the risk of venous thrombosis; using below-knee graduated compression stockings and avoiding restrictive clothing may also be helpful.

- Wear seat belts continuously to protect against injury from unexpected turbulence.

Women with medically or obstetrically complicated pregnancies that may be exacerbated by flight conditions or require emergency care should avoid air travel. Supplemental oxygen may be administered to pregnant women who must travel and may not tolerate the relatively hypoxic environment of high altitude flying, even in pressurized aircraft. (See "Evaluation of patients for supplemental oxygen during air travel".)

The amount of cosmic radiation received during airline travel is below the level at which there begins to be concern about possible harmful fetal effects (20 millisievert or 2 rem) [46]. As an example, a woman on a round trip transpolar flight from New York to Tokyo would be exposed to approximately 15 mrem cosmic radiation; for a round trip transcontinental flight across the United States, the exposure would be 6 mrem. In comparison, the International Commission on Radiological Protection (ICRP) and the National Council on Radiation Protection (NCRP) recommended limit for maximum cumulative radiation exposure for a member of the general public over one year is 100 mrem [47,48]. Pilots, flight attendants, and frequent fliers might exceed this level, particularly if they fly during solar particle events, when radiation levels can increase significantly. They should be aware of their personal radiation exposure, which can be

calculated using the Federal Aviation Administration Radiobiological Team web site. A detailed discussion of radiation risks in pregnancy can be found separately. (See "Diagnostic imaging in pregnant and nursing patients".)

Long-distance airline travel also disrupts circadian rhythms; the effects of this on pregnancy are unknown.

Travel to moderate and high altitudes

- **5000 to 8000 feet** – Airplane passenger cabins are usually pressurized to an altitude of 5000 to 8000 ft (1524 to 2438 m). The maternal PO_2 values at these altitudes are 132 and 118 mmHg, respectively (table 6) [45]. Pregnant women may be exposed to altitudes in this range from other sources, such as visiting a mountain resort or traveling in a hot air balloon or noncommercial aircraft. There is scant literature about acute, short-term exposure of pregnant women to these moderate altitudes. One study evaluated seven women in the third trimester at sea level (180 ft) and then within two to four days of visiting a facility at 6000 ft (1829 m) [45]. Plasma glucose rose from 4.53 to 5.51 mmol/L (81.6 to 99.2 mg/dL); maternal heart rate, oxygen consumption, ventilation, tidal volume, and plasma catecholamine and lactate levels did not change significantly, and there was no change in fetal heart rate.

  These data and other reports [49,50], although limited, are reassuring that women with uncomplicated pregnancies can tolerate acute exposure to moderate altitudes. Since an individual's altitude tolerance cannot be reliably determined at sea level, advice on travel to intermediate altitudes should err on the side of caution [49,50].

- **Over 8000 feet** – High altitudes (over 8000 ft [2438 m]) are more likely to cause problems. In general, exposure of a pregnant woman to the hypoxia induced by high altitudes results in acclimatization responses, which preserve the fetal oxygen supply. The fetus can also utilize some compensatory mechanisms during brief periods of hypoxia. However, these adaptive mechanisms may not be fully compensatory in complicated pregnancies, such as those with uteroplacental insufficiency, or at very high altitudes [51]. As an example, pregnancy in inhabitants of Cerro de Pasco, Peru (altitude 14,337 ft [4370 m]), is associated with 31 percent lower maternal cardiac output and 11 percent lower birth weight than observed in pregnant women residing at sea level (mean birth weight 2935 and 3290 g, respectively) [52].

  A survey of obstetric care providers in Colorado reported that preterm labor and bleeding complications of pregnancy were the most commonly encountered pregnancy complications among pregnant visitors to high altitudes [53]. Dehydration, engaging in

strenuous exercise before acclimatization, and participation in activities with high risk of trauma were behaviors that could increase the risk of pregnancy complications. Some experts suggest that an altitude of 8000 ft should not be exceeded in the first few days of short-term exposure to high altitude [49]. (See "High altitude illness: Physiology, risk factors, and general prevention".)

Hair dyes and other cosmetic products — Exposure to hair dyes or hair grooming/styling products results in very limited systemic absorption unless the integrity of scalp skin is compromised by disease. Therefore, these chemicals are unlikely to cause adverse fetal effects in women with a normal scalp [54,55]. Although adverse effects have been reported, data on safety are limited, inconsistent, and based on maternal self-report [56-58].

We tell patients that plant-based hair dyes are probably safe and there is no information on whether non-ammonia versus ammonia-based products are safer. A prudent approach is to avoid ammonia- and peroxide-based products, given the wide availability of non-ammonia-based products. We also tell patients to use these products in a well-ventilated area since women with asthma/allergies may be more sensitive to the scents during pregnancy. Lastly, it is prudent to avoid new products since skin sensitivity is more common in pregnancy.

There are also only limited data on the safety of cosmetics. As above, skin may be more sensitive in pregnancy. Some nail polishes have toluene, formaldehyde, and dibutyl phthalate. Theoretically, these toxins may be inhaled when applied or absorbed from the nail bed, so it is prudent to apply nail polish in a well-ventilated place.

Shortness of breath — Pregnancy is a state of relative hyperventilation, which appears to be centrally mediated through progesterone. The respiratory rate does not change while tidal volume increases, resulting in an approximately 50 percent increase in minute ventilation, which accounts for the feeling of shortness of breath. Physiologic dyspnea of pregnancy is of gradual onset: Sudden onset or presence of cough, wheezing, rales, chest pain, fever, or hemoptysis suggests a pathologic process that requires further evaluation. (See "Maternal adaptations to pregnancy: Dyspnea and other physiologic respiratory changes", section on 'Approach to differential diagnosis'.)

Airborne pollutants — Numerous studies have examined potential associations between various airborne pollutants and adverse outcomes, such as low birth weight, preterm birth, and small for gestational age infant, and have come to different conclusions because of difficulties in measuring exposures, timing of measurements, and degree of adjustment for confounding. (See "Occupational and environmental risks to reproduction in females: Specific exposures and impact", section on 'Air pollution'.)

Use of insect repellants — The CDC has advised pregnant women to take precautions to reduce their risk of acquiring arboviral infections (eg, Zika virus, West Nile virus, malaria) by avoiding mosquito bites through use of protective clothing (including permethrin-treated) and DEET (N,N-diethyl-3-methylbenzamide)-based repellents [59]. Topically applied DEET does not pose hazards to the developing fetus, regardless of gestational age. (See "Prevention of arthropod and insect bites: Repellents and other measures", section on 'Pregnant women' and "Prevention of arthropod and insect bites: Repellents and other measures", section on 'Permethrin-treated clothing'.)

Stretch marks and other normal changes of skin, nails, and hair — (See "Maternal adaptations to pregnancy: Skin, hair, nails, and mucous membranes".)

Tattoos and body piercing — (See "Maternal adaptations to pregnancy: Skin, hair, nails, and mucous membranes", section on 'Tattoos and piercing'.)

Management of common discomforts

Nausea and vomiting — Almost all pregnant women experience nausea with or without vomiting in early pregnancy, and a minority experience the severe end of the spectrum, hyperemesis gravidarum. (See "Nausea and vomiting of pregnancy: Clinical findings and evaluation" and "Nausea and vomiting of pregnancy: Treatment and outcome".)

Gastroesophageal reflux disease — Gastroesophageal reflux disease affects 40 to 85 percent of pregnant women. (See "Medical management of gastroesophageal reflux disease in adults", section on 'Pregnancy and lactation'.)

Constipation — The prevalence of constipation ranges from 16 to 39 percent in each trimester of pregnancy and 6 to 12 weeks postpartum. Constipation is common in pregnancy because of hormonal (progesterone) and mechanical factors. Increasing dietary fiber and fluids or using bulk-forming laxatives are the preferred treatments of constipation during pregnancy since these agents are not absorbed. For refractory cases, occasional use of magnesium hydroxide, lactulose, or bisacodyl is probably not harmful since magnesium salts have been widely used in pregnancy with a good safety profile and lactulose and bisacodyl, although not studied in human pregnancy, are minimally absorbed. Castor oil can stimulate uterine contractions, and excessive use of mineral oil can interfere with absorption of fat-soluble vitamins, so these agents are generally avoided. (See "Management of chronic constipation in adults".)

Hemorrhoids — Approximately 30 to 40 percent of pregnant or postpartum women are affected by hemorrhoidal discomfort. (See "Maternal adaptations to pregnancy: Gastrointestinal

tract", section on 'Hemorrhoids' and "Home and office treatment of symptomatic hemorrhoids".)

Rhinitis and epistaxis — Twenty to 30 percent of pregnant women develop symptomatic nasal congestion during pregnancy, a condition called pregnancy rhinitis (or rhinitis of pregnancy). Pregnant women also often experience epistaxis, possibly as a result of hyperemia of the nasal mucosa. (See "An overview of rhinitis", section on 'Rhinitis of pregnancy' and "Approach to the adult with epistaxis".)

Gingivitis — Most pregnant women note gingival changes and/or gingivitis (picture 1). These changes consist of enlargement and blunting of the interdigital papillae, which may result in gingival bleeding, ulceration, and pain. In addition to good oral hygiene, therapy for pregnancy gingivitis involves debridement and possibly adjunctive antibiotics. (See "Overview of gingivitis and periodontitis in adults", section on 'Non-plaque-associated gingivitis and gingival disease'.)

Difficulty sleeping — Sleep during pregnancy, especially late pregnancy, is fragmented and characterized by increased waking after sleep onset, greater amounts of light sleep, and less deep sleep [60-62]. Some reasons for this include nocturia, nocturnal gastroesophageal reflux, anxiety, restless legs or leg cramps, low back pain, physical limitations in achieving a comfortable position, and, primarily in obese women, obstructive sleep apnea. Interestingly, an individual patient meta-analysis found women with greater than average restless sleep had fewer stillbirths [63]. (See "Obstructive sleep apnea in pregnancy".)

In the absence of treatment for a specific medical condition, such as gastroesophageal reflux disease, suggestions for better sleep include maintaining a regular sleep schedule in a low stimuli environment; cutting down on the amount of liquids in the hours before bedtime; avoiding caffeine after noon; exercising regularly for at least 20 minutes at least a few hours before bedtime; placing pillows between the knees, under the abdomen, and behind the back to take pressure off the lower back; putting a night light in the bathroom to avoid turning on a bright light, which tends to increase wakefulness; using relaxation techniques; and avoiding naps late in the day [64]. Patients with chronic insomnia may benefit from cognitive behavioral therapy for insomnia. (See "Overview of the treatment of insomnia in adults", section on 'Pregnancy'.)

We do not prescribe sleep medication for pregnant women. Sedating antihistamines (eg, doxylamine, diphenhydramine) or zolpidem have been used for short-term treatment of sleeplessness in pregnancy. A 2015 systematic review and meta-analysis of 16 studies evaluated the use of benzodiazepines, hypnotic benzodiazepine receptor agonists, antidepressants, and

antihistamines in pregnant women with sleep disturbances [65]. Overall, the studies reported no correlation between use of these medications and risk of congenital anomalies. Benzodiazepines and hypnotic benzodiazepine receptor agonist use may increase the rates of preterm birth, low birth weight, and small for gestational age infants, but available studies were prone to bias. There is also concern that transplacental passage of these medications may cause neonatal respiratory depression. Although the meta-analysis was limited by the small number of studies, study design (most were cohort studies), and small numbers of included subjects, it generally supports avoiding such medications in pregnancy.

Headache — Headache is a common problem in reproductive-age women. Some types of headache (eg, migraine) can become less symptomatic in pregnant women because they are affected by hormonal fluctuations, while others (eg, tension, cluster) are not affected by the pregnant state. Headache can be a symptom of severe preeclampsia. (See "Headache in pregnant and postpartum women".)

Back pain — Over 60 percent of pregnant women report back pain at some point during the gestation. It is usually due to mechanical factors resulting from altered posture, muscle weakness, joint laxity, and/or vertebral facet joint irritation. (See "Maternal adaptations to pregnancy: Musculoskeletal changes and pain", section on 'Low back pain and disc disease'.)

Leg cramps and restless legs syndrome — Up to 50 percent of pregnant women experience leg cramps, especially in the third trimester, and up to 25 percent of pregnant women experience restless legs syndrome.

- (See "Maternal adaptations to pregnancy: Musculoskeletal changes and pain", section on 'Leg and foot pain'.)
- (See "Clinical features and diagnosis of restless legs syndrome and periodic limb movement disorder in adults", section on 'Pregnancy' and "Treatment of restless legs syndrome and periodic limb movement disorder in adults", section on 'Pregnancy and lactation'.)

Peripheral edema — Water retention is a physiological phenomenon in pregnancy, with an average increase at term of 3 L. Water retention is clinically evident as edema of the ankles and legs, a normal finding in a large proportion of pregnant women near term. A fall in plasma osmolality of 10 mOsmol/kg is one of the main reasons for water retention. Antidiuretic hormone release and the osmotic threshold for thirst decrease in parallel resulting in water retention [66].

Interventions that may prevent or reduce edema include not standing for long periods of time, resting/sleeping on the left side, wearing support hose or compression stockings, and water

immersion.

Varicose veins — Pregnancy is a risk factor for development of varicose veins, which affect up to 40 percent of pregnant women and may become symptomatic any time during the antepartum or postpartum period. Compression stockings do not prevent varicose veins, but they may relieve symptoms [67]. (See "Overview of lower extremity chronic venous disease" and "Vulvovaginal varicosities and pelvic congestion syndrome".)

Diarrhea — Diarrhea is a relatively common problem but probably not more common in pregnancy. The management of patients with acute diarrhea initially involves general supportive measures such as hydration and alteration of diet. Loperamide was not teratogenic in animal studies, but human data are conflicting [68]. Antibiotic therapy is rarely needed since the illness is usually self-limited and most often viral in etiology. (See "Approach to the adult with acute diarrhea in resource-rich settings".)

Urinary frequency and nocturia — Urinary frequency (voiding >7 times per day) and nocturia (voiding ≥2 times at night) are among the most common pregnancy-related complaints, affecting 80 to 95 percent of women at some point during gestation [69-71]. Frequency appears to be due in part to changes in bladder function and in part to a small increase in urine output. Urinary frequency typically begins in the first trimester; thus, mechanical compression of the bladder by the enlarged uterus is not likely to be the primary cause. Nocturia is common and increases with advancing gestation, which may be partially attributable to nocturnal mobilization of dependent edema. Supportive care includes avoiding caffeine and avoiding consumption of fluids two to three hours before bedtime. (See "Maternal adaptations to pregnancy: Renal and urinary tract physiology", section on 'Symptoms'.)

True polyuria, defined as urine output exceeding 3 L/day, is not physiologic and may be due to transient diabetes insipidus of pregnancy, which is a rare, but important cause of pathologic polyuria. (See "Polyuria and diabetes insipidus of pregnancy".)

SAFETY OF SELECTED COMMON MEDICATIONS USED TRANSIENTLY IN PREGNANCY

Overview — Medication use is common in pregnancy [72-77]. However, information about known or potential maternal or fetal adverse reactions and dose adjustments needed during pregnancy and the postpartum period is very limited because pregnant women are generally not included in studies to determine safety and efficacy of new medications. Furthermore, the background risk that a child will have a major congenital anomaly is 2 to 4 percent. Therefore, a

study would require 200 pregnancies exposed to a drug during the first trimester to provide sufficient power (80 percent at 5 percent significance level) to exclude an overall increase in risk of birth defects >3-fold higher than the background risk, and 700 such pregnancies would be needed to exclude an overall increase in risk >2-fold higher than the background risk [78]. Thousands of exposed pregnancies would be required to exclude an increased risk for a specific anomaly since the background risk of a specific anomaly is much less (eg, incidence of at least moderately severe congenital heart defects 6.5/1000 births [79]). It has been estimated that sufficient information to determine the risk for birth defects is available for <10 percent of medications approved by the US Food and Drug Administration (FDA) since 1980 [80]. It should also be noted that cautious interpretation of results is warranted due to potential confounding by indication for use of the drug and, in retrospective studies, recall bias.

The following general principles apply to use of medication during pregnancy:

- Avoid fetal drug exposure, when possible. The first trimester especially since it is the major period of organogenesis, but fetal exposure to drugs later in gestation can also result in subtle morphologic abnormalities, functional abnormalities, and impairment in growth.

- When a medication needs is to be taken, discuss with patients the risks and benefits of taking versus not taking the drug, citing the best available evidence. Information on the use of specific drugs in pregnancy is available in the UpToDate drug database, as well as in topics that review treatment of medical conditions in pregnant women. Other resources include:

    - Reproductive Toxicology Center
      REPROTOX
      Columbia Hospital for Women Medical Center
      Washington, DC
      202-293-5137

    - Teratogen Information System
      TERIS and Shepard's Catalog of Teratogenic Agents
      Seattle, WA
      206-543-2465

    - Pregnancy Exposure Registries

    - Organization of Teratology Information Specialists (OTIS)
      877-311-8972

- The Teratology Society
  The Teratology Society publishes a free teratology primer

- When prescribing drugs, minimize the number of medications taken, limit use of medication to situations where the benefit clearly outweighs the risk, choose medications with the best safety profile, and use them at the lowest dose and for the shortest duration that is effective. Older medications with good safety records are generally preferable to newer medications since pregnancy data on newer drugs are usually very limited or nonexistent.

- Inform patients to contact their provider with any medication concerns and before stopping a drug or starting a new drug (prescription, over-the-counter, or herbal [alternative] remedies).

Women exposed to drugs of uncertain safety in the first trimester can be offered ultrasound examination at 18 to 20 weeks of gestation to screen for fetal anatomic abnormalities, with fetal echocardiography if congenital heart disease is suspected. (See "Congenital heart disease: Prenatal screening, diagnosis, and management".)

Pain and fever medications

Acetaminophen — Acetaminophen is a widely used for treatment of pain and fever, with no high-quality evidence in humans of increased risk of pregnancy loss, congenital anomalies, or neurodevelopmental delay [81,82]. Epidemiologic studies have reported an association between in utero acetaminophen exposure and risk of attention-deficit/hyperactivity disorder (ADHD)-like behaviors in offspring [83]. However, the absolute risk was small and these studies had several methodologic limitations including a lack of assessment of overall health of the parents and index pregnancy; lack of information on acetaminophen strength, dose, and duration of use; and lack of formal assessment of ADHD.

A 2015 FDA Drug Safety Communication assessed the available evidence to be inconclusive regarding a possible connection between acetaminophen use in pregnancy and ADHD in children [84]. Similarly, a 2017 review by the Society for Maternal-Fetal Medicine reported that no conclusion could be made regarding a possible causal association between maternal acetaminophen use and neurobehavioral issues because of aforementioned study limitations [85]. Subsequent to these communications, a study from Norway that adjusted for maternal use of acetaminophen before pregnancy, familial risk for ADHD, and indications of acetaminophen use reported an increased risk of ADHD with acetaminophen use >29 days: hazard ratio (HR) 2.20 (95% CI 1.50-3.24), while use for <8 days was negatively associated with ADHD: HR 0.90 (95% CI 0.81-1.00) [86]. Moreover, paternal and maternal use of acetaminophen

were similarly associated with ADHD. These data may reassure women who require only a few doses of acetaminophen for treatment of fever or pain during pregnancy.

Epidemiologic studies have also suggested a small, but statistically significant, association between maternal use of mild analgesics and cryptorchidism in offspring, particularly second trimester or prolonged exposure [87-89]. Acetaminophen may also reduce fetal testosterone production. These findings are subject to the many limitations of observational studies and should not change practice, but they provide impetus for further research [84,90]. As with most other drugs, it is reasonable to avoid prolonged use of acetaminophen in pregnancy, if possible, until more data are available. Since descent of the testes occurs in late gestation, first trimester avoidance of acetaminophen will not address this potential problem.

An analysis of case reports of transient fetal ductus arteriosus constriction or closure suggested a possible association with maternal acetaminophen intake [91], but a subsequent cohort study concluded this risk was negligible (0 cases in 604 third-trimester exposures and 0 cases in 1192 first- and/or second-trimester exposures) [92]. Given the widespread use of the drug in pregnancy and the paucity of case reports, if this is a true association, it is extremely rare and not obviously causally related [93].

A single study reported a modest association between prepregnancy use of acetaminophen and birth of a small for gestational age infant, but no association with use during pregnancy [94]. It is possible that personal factors leading to high prepregnancy use of acetaminophen account for the association.

It is possible that reduction of fever with acetaminophen reduces the risk of some birth defects, but further study is needed [82]. The extensive use of acetaminophen by pregnant women combined with the paucity of documented adverse effects has served to make this medication the pain reliever and antipyretic of choice during pregnancy when short-term drug therapy is indicated [95].

However, it is important to caution patients against excessive use of acetaminophen. The therapeutic dose is 325 to 1000 mg per dose in adults, with a usual maximum recommended daily dose of approximately 3 g for oral immediate release preparations. Accidental overuse may be more likely in pregnancy due to limitations on use of other medications and perceptions of its safety. Limited data suggest good fetal outcomes in cases of maternal overdose/overuse, but potential for maternal morbidity is high. (See "Acetaminophen (paracetamol) poisoning in adults: Pathophysiology, presentation, and evaluation" and "Acetaminophen (paracetamol) poisoning in adults: Treatment", section on 'Treatment in pregnancy'.)

NSAIDs — The risks and benefits of using nonsteroidal anti-inflammatory drugs (NSAIDs) for treatment of pain or fever depend on the dose, gestational age, and duration of therapy. These risks are discussed in detail separately. Importantly, use of NSAIDs other than low dose aspirin for more than 48 hours can cause in utero constriction of the ductus arteriosus as early as 24 weeks of gestation, but is most common after 31 to 32 weeks. After 20 weeks, NSAIDs also have effects on the fetal kidneys that can lead to oligohydramnios, typically after at least 48 hours of therapy. (See "Safety of rheumatic disease medication use during pregnancy and lactation" and "Inhibition of acute preterm labor", section on 'Cyclooxygenase inhibitors (eg, indomethacin)'.)

Opioids — There is limited information on the effects of long-term (≥1 month) prescription opioid use during pregnancy. Maternal physiologic dependence and neonatal withdrawal syndrome are major concerns with long-term maternal opioid use that includes the week before delivery. For women with moderate to severe pain, opioids should be prescribed only when alternative pain management therapies are, or are likely to be, ineffective [96,97]. In a nationwide retrospective cohort study in the United States, 4 percent of women (379/9429) who were opioid-naïve in the year prior to pregnancy and filled an opioid prescription during pregnancy developed new persistent opioid use postpartum [98]. (See "Neonatal abstinence syndrome".)

The safety of short-term opioid use is also unclear. Data from an animal study support an association between maternal opioid use and central nervous system defects in offspring [99]. Three epidemiologic studies in humans have also reported an association with neural tube defects, with odds ratios (OR) of 1.7 to 2.9 [100-102]. An association has also been reported between opioid use in pregnancy and congenital heart defects, and gastroschisis; preterm delivery, poor fetal growth, and stillbirth [100,103]. In most cases, opioids were used for short-term analgesia. Limitations of these studies include that exposure information was based on maternal recall up to one year after delivery, information on drug dose and duration was not obtained, the drugs were used to treat pain from a wide variety of disorders, many of the narcotics were part of a multi-component drug regimen, congenital abnormalities in pregnancy losses were not ascertained, and the possibility of chance associations is increased when multiple comparisons are made. Even in the large studies, the number of cases was small and subject to selection bias. A 2015 FDA Safety Announcement stated further investigation of this issue is needed before we can determine whether the weight of evidence supports the presence of an increased risk of neural tube defects related to opioid exposure in early pregnancy [84]. The absolute risk of open neural tube defects is low in the United States, approximately 3 per 10,000 live births. Therefore, if a true causal relationship exists, a twofold increase in risk would represent a small increase in the absolute risk of open neural tube defects.

Until better data are available, during the first month of embryonic development when neural tube development occurs, shared decision-making involves balancing the small potential increase in incidence of neural tube defects with the need for relief of moderate to severe pain, given the frequent lack of effective alternative analgesics.

Issues related to methadone and nonprescription opioids are reviewed separately. (See "Substance use during pregnancy: Screening and prenatal care" and "Overview of management of opioid use disorder during pregnancy" and "Methadone and buprenorphine pharmacotherapy of opioid use disorder during pregnancy".)

Antibiotics — Antibiotics without known teratogenic effects include the cephalosporins, the penicillins, clindamycin, amoxicillin-clavulanate, and metronidazole.

The following antibiotics have been associated with known or potential teratogenic effects:

- **Aminoglycosides** carry a risk of fetal (and maternal) ototoxicity and nephrotoxicity, but not with structural birth defects.

- Doxycycline – Tetracyclines are generally contraindicated in pregnancy because of the risk of hepatotoxicity in the mother [104] and adverse effects on fetal bone and teeth (eg, permanent discoloration of deciduous teeth from in utero exposure in the second and third trimesters [105], incorporation into fetal long tubular bones with transient inhibition of growth [106]). However, these events are extremely rare with doxycycline, in part because it binds less readily to calcium than other tetracycline antibiotics. The body of evidence in both pregnancy and in children has supported the relative safety of doxycycline compared with older tetracyclines [107-109]. As an example, in a systematic review, there was no correlation between the use of doxycycline and teratogenic effects during pregnancy or dental staining in children (no doxycycline-associated adverse events in 2049 exposures, except for one case with slight discoloration of upper incisors) [107]. However, data are low quality and insufficient to conclude that there is no risk. If there is a safer, effective drug that can be used as an alternative, it should be used. But if there is no good alternative (eg, Rocky Mountain spotted fever), doxycycline should be used rather than tetracycline. Of note, the 2018 Red book stated that doxycycline can be used for ≤21 days in children of all ages.

- **Fluoroquinolones** – Fluoroquinolones are generally avoided during pregnancy and lactation because they are toxic to developing cartilage in experimental animal studies. Neither adverse effects on cartilage nor an increase in congenital malformations from use during human pregnancy has been documented in meta-analyses, but available data are limited [110,111].

- Trimethoprim – Trimethoprim is generally avoided in the first trimester because it is a folic acid antagonist [112-114], has caused abnormal embryo development in experimental animals, and some case control studies have reported a possible association with a variety of birth defects [81]. However, it is not a proven teratogen in humans. Additional evaluation of the safety of trimethoprim in human pregnancy is needed. The safest course is to avoid using trimethoprim in the first trimester if another antibiotic that is safe and effective is available. If exposure does occur, we advise patients of the baseline risk of birth defects in the population and the possibility of a low, but unproven increase in risk of birth defects after exposure to trimethoprim.

- **Sulfonamides,** nitrofurantoin – The safest course is to avoid using nitrofurantoin or sulfonamides in the first trimester if another antibiotic that is safe and effective is available, but use of these drugs is appropriate when good alternatives are not available, based on the data discussed below [115]. Both drugs have been implicated to cause hemolysis in women with glucose-6-phosphate dehydrogenase deficiency and those at risk for this condition (table 7), although the literature contains conflicting information. (See "Diagnosis and management of glucose-6-phosphate dehydrogenase (G6PD) deficiency", section on 'Inciting drugs, chemicals, foods, illnesses'.)

  In a meta-analysis of 10 studies with a total of over one million participants, maternal exposure to sulfonamides was possibly associated with an increased risk of congenital malformations (OR 1.21, 95% CI 1.07-1.37) [116]. However, data were retrospective and long periods between the exposure and patient interviews could bias results, data on specific abnormalities were limited, neither true exposure nor whether exposure occurred in the first versus second versus third trimester could be ascertained accurately, some mothers were taking more than one drug and mothers taking sulfonamides could be taking any of five formulations, and the effects of the underlying infection versus the effects of the sulfonamides could not be distinguished.

  Sulfonamides compete with bilirubin for albumin binding sites and theoretically may increase the risk of kernicterus at low bilirubin levels. For this reason, these drugs have been avoided near delivery if another antibiotic is available. However, a systematic review found no cases of kernicterus associated with maternal use of sulfonamides during pregnancy or lactation [117]. A subsequent study reported the presumed association between maternal use of sulfamethizole and neonatal jaundice was the result of preterm birth; the association became insignificant when data were adjusted for gestational age [118]. Another study described an increased risk of kernicterus in preterm infants administered sulfisoxazole for antibiotic prophylaxis [119].

- Fluconazole – First-trimester exposure to high-dose fluconazole therapy (400 to 800 mg/day) appears to be teratogenic, but the magnitude of the teratogenic risk is unknown. The impact of low-dose fluconazole exposure is unclear but more reassuring. Available data are reviewed separately. (See "Candida vulvovaginitis: Treatment", section on 'Pregnancy'.)

- **Macrolides** – A 2019 systematic review reported an association between macrolides and miscarriage [120]. In a cohort study evaluating outcomes of over 100,000 children whose mothers were prescribed macrolide monotherapy (erythromycin [n = 7987], clarithromycin [n = 494], or azithromycin [n = 151]) or one penicillin monotherapy (n = 95,973) from the fourth gestational week to delivery, macrolide prescribing in the first trimester was associated with increased risks of any major malformation compared with penicillin (27.65 versus 17.65/1000, adjusted risk ratio [RR] 1.55, 95% CI 1.19-2.03) and cardiovascular malformations (10.60 versus 6.61/1000, adjusted RR 1.62, 95% CI 1.05-2.51) [121]. Macrolide prescribing in any trimester was associated with an increased risk of genital malformations, mainly hypospadias (4.75 versus 3.07/1000, adjusted RR 1.58, 95% CI 1.14-2.19).

  The clinical implications of these findings remain uncertain. Three-quarters of the prescriptions were for respiratory tract infection. Confounding by indication and unmeasured confounders could account for the results, the absolute risk of a congenital anomaly is low, and macrolides are most commonly administered to pregnant women for indications (eg, surgical prophylaxis, prolonging latency after rupture of membranes) that occur after organogenesis (formation of the heart and urethra are complete by 9 and 18 weeks of gestation, respectively).

Additional detail for these and other antibiotics is available by searching the UpToDate drug information program for the specific antibiotic and reviewing the specific drug's section on Pregnancy Implications. Also, the choice of antibiotic and the risks and benefits of use of specific antibiotics in specific infections are discussed in the UpToDate topics on the specific infections. For example, use of doxycycline for treatment of pregnant women with Rocky Mountain spotted fever is discussed in the following topic. (See "Treatment of Rocky Mountain spotted fever", section on 'Pregnant women'.)

Cold and allergy medications — Use of over-the-counter and prescription drugs for treatment of respiratory infections and allergies in pregnancy is discussed in detail elsewhere. (See "Treatment of respiratory infections in pregnant patients" and "Recognition and management of allergic disease during pregnancy".)

Medications for treatment of nausea and vomiting — (See "Nausea and vomiting of pregnancy: Treatment and outcome".)

PREPARATION FOR LABOR, DELIVERY, AND THE PUERPERIUM

- (See "Preparation for childbirth".)
- (See "Breastfeeding: Parental education and support".)
- (See "Postpartum contraception: Counseling and methods".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Prenatal care".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Prenatal care (The Basics)" and "Patient education: Activity during pregnancy (The Basics)")

- Beyond the Basics topics (see "Patient education: Avoiding infections in pregnancy (Beyond the Basics)" and "Patient education: Should I have a screening test for Down syndrome during pregnancy? (Beyond the Basics)" and "Patient education: Group B streptococcus and pregnancy (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Patient education and health promotion are important components of prenatal care and involve discussion of various subjects. (See 'Patient education and health promotion' above.)
- The following general principles apply to use of medication during pregnancy (see 'Safety of selected common medications used transiently in pregnancy' above):
  - Avoid fetal drug exposure, when possible, especially the first trimester since it is the major period of organogenesis, but fetal exposure to drugs later in gestation can also result in subtle morphologic abnormalities, functional abnormalities, and impairment in growth.
  - When a medication needs is to be taken, discuss with patients the risks and benefits of taking versus not taking the drug, citing the best available evidence. Information is available from several resources.

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Topic 112420 Version 55.0

GRAPHICS

US Food and Drug Administration advice on fish consumption in women who are pregnant, might become pregnant, or are nursing

Best choices (eat 2 to 3 servings a week)		
▪ Anchovy ▪ Atlantic croaker ▪ Atlantic mackerel ▪ Black sea bass ▪ Butterfish ▪ Catfish ▪ Clam ▪ Cod ▪ Crab ▪ Crawfish ▪ Flounder ▪ Haddock	▪ Hake ▪ Herring ▪ Lobster (American and spiny) ▪ Mullet ▪ Oyster ▪ Pacific chub mackerel ▪ Perch (freshwater and ocean) ▪ Pickerel ▪ Plaice ▪ Pollock ▪ Salmon ▪ Sardine	▪ Scallop ▪ Shad ▪ Shrimp ▪ Skate ▪ Smelt ▪ Sole ▪ Squid ▪ Tilapia ▪ Trout (freshwater) ▪ Tuna, canned light (includes skipjack) ▪ Whitefish ▪ Whiting
Good choices (eat 1 serving a week)		
▪ Bluefish ▪ Buffalofish ▪ Carp ▪ Chilean sea bass/Patagonian toothfish ▪ Grouper ▪ Halibut ▪ Mahi mahi/dolphinfish	▪ Monkfish ▪ Rockfish ▪ Sablefish ▪ Sheepshead ▪ Snapper ▪ Spanish mackerel ▪ Striped bass (ocean)	▪ Tilefish (Atlantic Ocean) ▪ Tuna, albacore/white tuna, canned and fresh/frozen ▪ Tuna, yellowfin ▪ Weakfish/sea trout ▪ White croaker/Pacific croaker
Choices to avoid (highest mercury levels)		
▪ King mackerel ▪ Marlin ▪ Orange roughy ▪ Shark	▪ Swordfish ▪ Tilefish (Gulf of Mexico) ▪ Tuna, bigeye	

One serving can be considered 3.5 ounces (100 grams). Note: On average, farm-raised fish tend to be lower in mercury compared with wild-caught fish[1].

Reference:

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Reproduced from: US Food and Drug Administration. Food: Eating Fish: What Pregnant Women and Parents Should Know. Available at: http://www.fda.gov/Food/FoodborneIllnessContaminants/Metals/ucm393070.htm (Accessed January 26, 2017).

Graphic 111607 Version 5.0

Recommendations for total and rate of weight gain for singleton pregnancies by prepregnancy BMI

	Total weight gain		Rates of weight gain* second and third trimester	
Prepregnancy BMI	**Range in kg**	**Range in lb**	**Mean (range) in kg/week**	**Mean (range) in lb/week**
Underweight (<18.5 kg/m^2)	12.5 to 18	28 to 40	0.51 (0.44 to 0.58)	1 (1 to 1.3)
Normal weight (18.5 to 24.9 kg/m^2)	11.5 to 16	25 to 35	0.42 (0.35 to 0.50)	1 (0.8 to 1)
Overweight (25.0 to 29.9 kg/m^2)	7 to 11.5	15 to 25	0.28 (0.23 to 0.33)	0.6 (0.5 to 0.7)
Obese (≥30.0 kg/m^2)	5 to 9	11 to 20	0.22 (0.17 to 0.27)	0.5 (0.4 to 0.6)

Recommended weight gain is higher for women with multiple gestations.

BMI: body mass index.
* Calculations assume a 0.5 to 2 kg (1.1 to 4.4 lb) weight gain in the first trimester.

Weight Gain During Pregnancy: Reexamining the Guidelines. Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines, Rasmussen KM, Yaktine AL (Eds), National Academies Press (US), The National Academies Collection: Reports funded by National Institutes of Health, Washington (DC) 2009. Reprinted with permission from the National Academies Press, Copyright © 2009 National Academy of Sciences.

Graphic 75820 Version 18.0

Immunizations that may be administered before, during, and after pregnancy[1,2]

Vaccine	Before pregnancy	During pregnancy	After pregnancy	Type of vaccine
Hepatitis A	Yes, if indicated	Yes, if indicated	Yes, if indicated	Inactivated
Hepatitis B	Yes, if indicated	Yes, if indicated*	Yes, if indicated	Inactivated
Human papillomavirus (HPV)	Yes, if indicated	No, delay until after pregnancy, if indicated	Yes, if indicated	Inactivated
Influenza IIV	Yes	Yes	Yes	Inactivated
Influenza LAIV¶	Yes, if less than 50 years of age and healthy; avoid conception for 4 weeks	No	Yes, if less than 50 years of age and healthy; avoid conception for 4 weeks	Live
MMR	Yes, if indicated, avoid conception for 4 weeks	No	Yes, if indicated, give immediately postpartum if susceptible to rubella	Live
Meningococcal:				
▪ Quadrivalent conjugate (MenACWY)	If indicated	If indicated	If indicated	Inactivated
▪ Serogroup B (MenB)	If indicated	No, delay until after pregnancy, if indicatedΔ	If indicated	Inactivated
Pneumococcal:				
▪ Polysaccharide	If indicated	If indicated	If indicated	Inactivated
Tdap	Yes, if indicated	Yes, vaccinate during each pregnancy ideally between 27 and 36 weeks of gestation	Yes, immediately postpartum, if not received previously	Toxoid/inactivated
Tetanus/diphtheria Td	Yes, if indicated	Yes, if indicated, Tdap preferred	Yes, if indicated	Toxoid
Varicella	Yes, if indicated, avoid conception for 4 weeks	No	Yes, if indicated, give immediately postpartum if susceptible	Live

LAIV: Live attenuated influenza vaccine; MMR: Measles, mumps, and rubella vaccine.
* Conventional recombinant hepatitis B vaccines should be used during pregnancy. Administration of the adjuvanted recombinant hepatitis B vaccine is not recommended during pregnancy because of lack of safety data.
¶ Confirm that LAIV is a recommended option for influenza vaccination each season.
Δ Delay MenB until after pregnancy unless at increased risk and vaccination benefit outweighs uncertain risks.

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Graphic 100422 Version 3.0

Women at increased risk of having a sexually transmitted infection

- Personal history of a prior sexually transmitted infection
- Age <25 years
- New sex partner in past 60 days
- More than one sex partner or sex partner with multiple concurrent sex partners
- Sex partner diagnosed with a sexually transmitted infection
- No or inconsistent condom use outside a mutually monogamous sexual partnership
- Trading sex for money or drugs
- Sexual contact with sex workers
- Meeting anonymous partners on the internet
- Unmarried status
- Lower socioeconomic status or high school education or less
- Admission to correctional facility or juvenile detention center
- Use of illicit drugs
- Living in a community with a high prevalence of sexually transmitted infections

Graphic 112388 Version 2.0

Signs and symptoms attributed to supine hypotensive syndrome in pregnancy

Faintness
Dyspnea
Dizziness
Restlessness
Nausea
Vomiting
Chest pain
Abdominal pain
Visual disturbances
Numbness
Paresthesias
Headache
Cold, clammy skin
Pallor
Cyanosis
Hypotension

Graphic 80135 Version 1.0

Physical effects of change in altitude

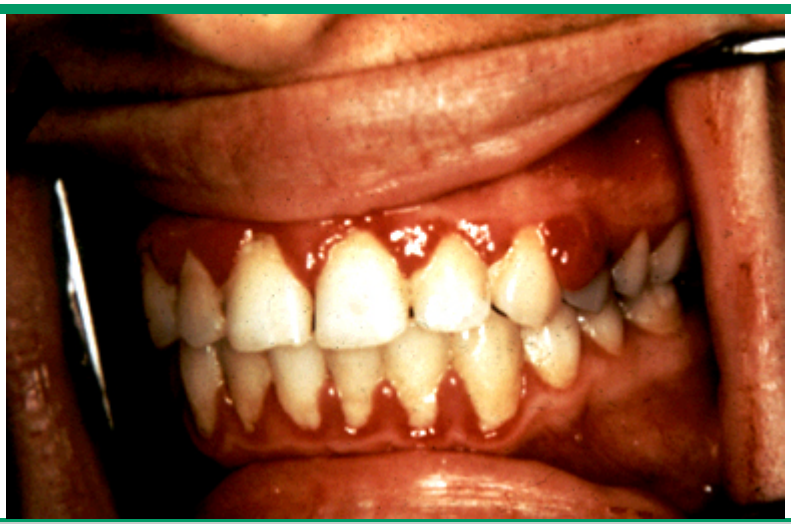
Altitude, feet	Barometric pressure, mmHg	Atmospheric PO_2, mmHg	PIO_2, mmHg	PAO_2, mmHg	PaO_2, mmHg
0	760	159	149	103	98
2000	707	148	138	94	90
4000	656	137	128	85	80
5000	632	132	122	81	66
6000	609	127	117	77	64
8000	564	118	108	69	60
10000	523	109	100	61	53

PIO_2: partial pressure of inspired oxygen; PAO_2: partial pressure of alveolar oxygen; PaO_2: partial pressure of oxygen in arterial blood
8000 feet represents the maximum allowable altitude in commercial aircraft.

Adapted from Gong H. Exposure to moderate altitude and cardiorespiratory diseases. Cardiologica 1995; 40:477.

Graphic 63773 Version 3.0

Gingivitis during pregnancy



Hormonal changes that occur with pregnancy significantly influence the bacterial flora, causing significant gingival inflammation and hypertrophy.

Courtesy of Mark S Obernesser, DDS, MMSc.

Graphic 82278 Version 1.0

Partial list of medicines and other substances thought to be unsafe or safe in individuals with G6PD deficiency

Medicines and other substances likely to be UNSAFE in moderate to severe G6PD deficiency*
Medications
Chlorpropamide
Dabrafenib
Dapsone (diaminodiphenyl sulfone)
Fluoroquinolones (ciprofloxacin, moxifloxacin, norfloxacin, ofloxacin)¶
Methylene blue (methylthioninium chloride)Δ
Nalidixic acid◊
Nitrofurantoin, nifuratel, and nitrofurazone (nitrofural)◊
Phenazopyridine (pyridium)
Primaquine and tafenoquine
Rasburicase and pegloticase
Sulfonylureas (eg, glipizide, glyburide [glibenclamide])
Chemical exposures and foods
Fava beans
Henna compounds (black and red Egyptian)
Naphthalene (mothballs, lavatory deodorant)
Phenylhydrazine
"RUSH" (isobutyl nitrate, amyl nitrate)
Medicines that are PROBABLY SAFE given in usual therapeutic doses in G6PD deficiency*; NOTE: some of these were previously considered unsafe; safety in Class I variants is generally not known
Acetaminophen (Tylenol, Paracetamol)
Aminophenazone, dipyrone, and metamizole (NSAIDs)◊
Antazoline (antihistamine)
Antipyrine (phenazone)
Ascorbic acid (vitamin C)
Aspirin (acetylsalicylic acid)
Benzhexol (Artane)
Chloramphenicol
Chloroquine and hydroxychloroquine
Colchicine
Clotrimazole
Diphenhydramine (Benadryl)
Isoniazid
Levodopa (L-Dopa) and levodopa-carbidopa
Para-aminosalicylic acid
Para-aminobenzoic acid (PABA)
Phenylbutazone
Phenytoin

Probenecid (Benemid)
Procainamide (Pronestyl)
Pyrimethamine (Daraprim)
Quinine
Streptomycin
Sulfa-containing drugs§ (sulfacetamide, sulfadiazine, sulfamethoxazole [Gantanol], trimethoprim-sulfamethoxazole, sulfamethoxypyridazine [Kynex], sulfanilamide, sulfisoxazole [Gantrisin])
Tiaprofenic acid
Trimethoprim
Tripelennamine (Pyribenzamine)
Vitamin K

This is a general list and may not apply to all G6PD-deficient individuals. Use clinical judgment, and refer to UpToDate discussions, patient history, and other resources for additional information.

G6PD: glucose-6-phosphate deficiency; NSAIDs: nonsteroidal antiinflammatory drugs.

* Applies to Class I, II, and III G6PD variants. However, note that there is marked variability in reports. This list is based on evidence supporting a clear association with drug-induced hemolysis. Individual characteristics (ie, degree of G6PD deficiency, dose, presence of infection) will determine actual safety or injury. Medicines known to be unsafe in G6PD deficiency that are no longer in clinical use are excluded from this list. In cases where the patient truly requires the medication and G6PD status is unknown, it may be appropriate to administer and monitor closely.
¶ Levofloxacin is not listed because some cases of hemolytic anemia with levofloxacin have been associated with a positive Coombs test.
Δ Methylene blue is a component of some combination urinary tract products.
◊ Not available in the United States.
§ Sulfamethoxazole is widely used. Some cases of hemolysis in individuals with G6PD deficiency have been reported. Use with caution.

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Graphic 74254 Version 24.0

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Charles J Lockwood, MD, MHCM Nothing to disclose **Urania Magriples, MD** Nothing to disclose **Vincenzo Berghella, MD** Consultant/Advisory Boards: ProtocolNow [Clinical guidelines]. **Vanessa A Barss, MD, FACOG** Nothing to disclose

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